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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/019,816	03/27/2002	Michael Valentine Agrez	SW-046 XX	9944

207 7590 04/12/2005

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EXAMINER	
CANELLA, KAREN A	
ART UNIT	PAPER NUMBER
1642	

DATE MAILED: 04/12/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/019,816	AGREZ ET AL.	
	Examiner	Art Unit	
	Karen A. Canella	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *217-221,223-225,236-238 and 240-263* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *217-221,223-225,236-238 and 240-263* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Claims 139, 141, 143-147, 150-152, 154, 163, 169, 171, 177, 193, 196, 197, and 222 have been canceled. Claims 247-263 have been added. Claims 217-221, 236, 240 and 244 have been amended. Claims 217-221, 223-225, 236-238 and 240-263 are examined on the merits.

Acknowledgement is made of applicant's election with traverse of Group 4, drawn to a method of modulating the activity of a cell comprising treating said cell with an effective amount of an agent that inhibits binding of a MAP kinase top the binding domain of an integrin for said MAP kinase. The traversal is on the grounds that the instant amended claims do not lack Unity of Invention because the cited art does not teach the instant embodiments. This has been considered and found persuasive because the instant claims are limited to method claims reliant on the direct binding of a MAP kinase with the cytoplasmic domain of an integrin, a feature which is novel over the prior art.

Acknowledgment is made to the foreign applications of PQ 1248 and PQ 8003. Although certified copies were submitted in the instant application, only the odd-numbered pages are present in the file. Further, the priority applications lack adequate written description for the instant method claims because the provisional applications contemplate the direct interaction between a Map kinase and the cytoplasmic domain of alph-v-beta6 which does not support the instant claims which depend on the interaction between a MAP kinase and any integrin. Accordingly for the purpose of the prior art search, the instant application was given the effective priority date of June 28, 2000.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the

specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention..

(A)As drawn to the disruption of the broadly claimed "integrins" and "MAP kinases"

The claims are broadly drawn to methods which encompass any integrin. It is noted that the priority document filed 28 June 1999 states that although no MAP kinase or any other subunit form of MAP kinase has been shown to bind to any of the 23 known integrins, the inventors have surprising determined that MAP kinase binds directly to the cytoplasmic domain of alpha-v-beta6 (page 2, lines 14-17). Thus it would be undue experimentation, without reasonable expectation of success to practice the broadly claimed methods which encompass any integrin, because the prior document actually teaches away from using the method with integrins beyond that of alpha-v-beta6. Further, claims 217-221, 223-225, 236-238, 240, 243, -252, 254-248 encompass MAP kinases which are not part of the ERK or JNK families. Claims 241 and 253 and 262 encompass members of the ERK family and JNK family beyond those of ERK2 and JNK1. The art recognizes that MAP kinases comprising three different families: the ERK, JNK and p38, and that individual members participate in different signaling cascades (Garington and Johnson, Current Opinion in Cell Biology, 1999, Vol. 11, pp. 211-218, reference of the IDS filed July 30, 2002, page 212, figure 1) and are regulated by different scaffolding proteins (ibid, page 213, figure 2). Because MAP kinases such as ERK3-5 and p38 are present in entirely different signaling cascades and are bound by different scaffolding proteins such as MP-1 which binds to ERK1 and JIP-1 or MEKK1 both of which lead to enhanced JNK activation, one of skill in the art would reasonably conclude that the binding of ERK1 or JNK directly to the cytoplasmic domain of alpha-v-beta6 did not provide a nexus for the binding of any MAP kinase directly to alpha-v-beta6 or any other integrin because the MAP kinases differ in protein-protein interactions with other known members in signaling cascades as exemplified by figure 2 of Garington and Johnson. Given the lack of objective evidence in the specification for the direct binding MAP kinases which were not ERK2 or JNK-1 to an integrin which was alpha-v-beta6 or any other integrin, one of skill in the art would be subject to undue experimentation in order to practice the broadly claimed method

(B)As drawn to agents which are not fragments of the cytoplasmic domain of alpha-v-beta6, or the peptides of SEQ ID NO:2, 2, 22 and 23.

Claims 217, 219-221, 223-225, 236-243, 246-247, 249-255, 257-263 are drawn to methods reliant on the identity of an "agent", or an agent which comprises a "polypeptide" or an analog or derivative thereof. The specification teaches agents which comprise the integrin-map kinase binding domain and the peptides of SEQ ID NO:2, 3, 22 and 23. When given the broadest reasonable interpretation the term "agent" is not limited in scope to molecules comprising the disclosed fragments of the integrin cytoplamic regions which binds to ERK2 or JNK-1 or to antibodies which bind to said cytoplasmic regions or the binding regions of ERK2 and JNK-1 that interact with the cytoplasmic domain of alpha-v-beta6. The specification does not provide teachings of how to make the genus of "agent" on which the instant method claims depend. Further, claims 218 and 245 are reliant on "analogs" and "derivatives" of the fragment of the integrin cytoplasmic domain that comprises the binding domain for the MAP kinases and analogs or derivatives of the core amino acid sequence which binds to a binding site of the Map kinase for the integrin. The specification defines the term "analog" as a molecule that has one or more aspects of biological function characteristic of the molecule on which at least part of the analog is based or which was otherwise utilized in the design or preparation of the analog. The specification states that an analog may have substantial overall structural similarity with the molecule or only structural similarity with one or more regions or domains thereof responsible for the desired characteristic biological function and that by "structural" similarity is meant similarity in shape, conformation and/or other structural features responsible for the provision of the biological function or which otherwise have involvement in the provision of the biological function. The specification states that it is not necessary that an analog have amino acid sequence homology, and an analog may not be proteinaceous at all. The specification state that "derivative" is a molecule that is derived or obtained from another molecule and which retains one or more aspects of characteristic biological function of that molecule. The specification has not taught how to make the structures of said analogs and derivatives that would function as claimed.

Given the lack of teachings in the specification regarding methods reliant on MAP kinases beyond those or EKR2 and JNK, the negative teachings of the p[priority document regarding the binding of MAP kinases to integrins other than alpha-v-beta6, and the lack of teachings in the specification regarding the making of the required "analogs" and "derivatives"

of the core amino acid sequence of the binding domain of the integrin, one of skill in the art would be subject to undue experimentation in order to practice the broadly claimed methods.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Karen A. Canella whose telephone number is (571)272-0828. The examiner can normally be reached on 10 a.m. to 9 p.m. M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeffrey Siew can be reached on (571)272-0787. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Karen A. Canella

Karen A. Canella, Ph.D.

4/4/2005